

Serial No.: 09/841,264

Confirmation No.: 5359

Filed: April 24, 2001

For: BIOLOGICAL SAMPLE PROCESSING METHODS AND COMPOSITIONS THAT INCLUDE
SURFACTANTS

Remarks

The Office Action mailed November 19, 2003 has been received and reviewed. No claims having been added, amended, or canceled, the pending claims are claims 1-50. Claims 25-50 having been withdrawn from consideration by the Examiner, the claims currently under consideration are claims 1-24. Reconsideration and withdrawal of the rejections are respectfully requested.

Obviousness-Type Double Patenting Rejection

Claims 1-24 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-45 of U.S. Pat. No. 6,617,136 B2.

Upon an indication of otherwise allowable subject matter and in the event this rejection is maintained, Applicants will provide an appropriate response.

Objection to Preliminary Amendment

The Examiner objected to the preliminary amendment submitted February 28, 2002, under 35 U.S.C. §132 for allegedly introducing new matter into the specification. Specifically, the Examiner alleged that added Figures 2-4 were not supported by the original disclosure. Applicants respectfully traverse the objection.

Applicants respectfully submit that Figures 2-4 are incorporated by reference in the original disclosure as described in the accompanying Declaration under 37 C.F.R. §1.132.

In view of the accompanying declaration, Applicants respectfully request that the Examiner reconsider and withdraw the objection to the preliminary amendment.

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Rejection under 35 U.S.C. §103

The Examiner rejected claims 1, 5-16, 20, and 23 under 35 U.S.C. §103(a) as being unpatentable over Park et al. (U.S. Patent No. 5,861,251) in view of Shultz et al. (U.S. Patent No. 6,242,235 B1) and Hayes et al. (U.S. Patent No. 5,721,123).

"To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure."

M.P.E.P. §706.02(j) citing *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Independent claim 1 (as well as independent claims 17, 18, and 19, which are not subject to this rejection) recites that a "dye inactivates the enzyme in the absence of the surfactant." Independent claim 20 (as well as independent claim 24, which is not subject to this rejection) recites the presence of a dye "under conditions that normally inactivate the enzyme." Applicants respectfully submit Park et al. in view of Shultz et al. and Hayes et al. fail to teach or suggest all the claim language including, for example, a composition in which a "dye inactivates the enzyme in the absence of the surfactant" (e.g., claims 1-19), or a method of stabilizing an enzyme in the presence of a dye "under conditions that normally inactivate the enzyme," wherein the method includes "combining an effective amount of a . . . surfactant . . . with the enzyme and the dye (e.g., claims 20-24). Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness for at least the reasons presented herein below.

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PARK ET AL. FAIL TO SUGGEST OR DISCLOSE A PCR REAGENT MIXTURE THAT INCLUDES THE COMBINATION OF A POLYMERASE, A DYE, AND A NONIONIC SURFACTANT

"A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention." M.P.E.P. §2141.02, citing *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).

For support of the rejection of claims 1, 5-16, 20, and 23 under 35 U.S.C. §103(a), the Examiner alleged that Park et al. "disclose a PCR reagent mixture containing a polymerase, a dye and a nonionic surfactant" (page 3, lines 23-24, of the Office Action mailed November 19, 2003), and pointed to column 3, lines 1-30 of Park et al. for specific support. Applicants respectfully disagree with the Examiner's characterization of Park et al.

Applicants note that the word "dye" does not even appear in column 3, lines 1-30 of Park et al. *Further, Applicants Representatives respectfully submit that no where in the specification of Park et al. is there a disclosure of a PCR reagent mixture containing the combination of a polymerase, a dye, and a nonionic surfactant.* The specification of Park et al. recites a disjointed collection of species that may be included in a reagent for PCR. Although the Examiner alleged that "[i]t is clear that all of the reagents disclosed by Park et al in col 3 for the PCR are reagents that can be used together in the PCR" (page 5, lines 17-19 of the Office Action mailed November 19, 2003), Applicants respectfully submit that the Examiner is improperly picking and choosing individually disclosed species to arrive at the presently claimed combination, with no disclosure from Park et al. to guide one of skill in the art to arrive at the presently claimed combination.

Specifically, Park et al. disclose that a "reagent for PCR . . . is prepared by freeze-drying a conventional aqueous reaction mixture which consists of a reaction buffer, MgCl₂, dNTPs and a DNA polymerase" (column 3, lines 3-7). "The PCR reagent of the invention may

further comprise a sedimenting agent or a water-soluble dye in the presence/absence of stabilizer" (column 3, lines 30-32). Thus, Park et al. clearly disclose a PCR reagent mixture containing the combination of a polymerase; a sedimenting agent *or* a water-soluble dye; and, optionally, a stabilizer.

The Examiner also alleged that "Park et al clearly teach that the dye can be used in the presence/absence of the *stabilizer which can be the surfactant* (col 3, lines 30-35)" (page 5, lines 19-21, of the Office Action mailed November 19, 2003, emphasis added). Applicants again disagree with the Examiner's characterization of Park et al., and respectfully submit that Park et al. fail to disclose or suggest that *a stabilizer can be a surfactant*.

The only recitation of the term *surfactant* by Park et al. is the isolated recitation that it has been well known that "non-ionic surfactants . . . improve the reactivity of the PCR mixture" (column 3, lines 18-20). However, Park et al. fail to disclose or suggest including such non-ionic surfactants in their disclosed PCR mixtures. Further, Park et al. clearly draw a distinction (e.g., column 3, lines 16-20) between materials that *stabilize a DNA polymerase and dNTPs* (e.g., "gelatin, BSA, Thesit (polyoxyethylene-9-lauryl ether), PEG-8000 (polyethyleneglycol-8000) or polyol (e.g., glycerol, glucose, mannitol, galacitol, glucitol and sorbitol)" as recited at column 3, lines 24-27) and *materials that improve the reactivity of a PCR mixture* (e.g., "non-ionic surfactants such as NP40 and Tween 20 etc. as recited at column 3, lines 18-20), thereby teaching away from the possibility that a stabilizer might function as a non-ionic surfactant. Park et al. also fail to provide guidance to one of skill in the art to select from the list of 10 recited stabilizers (e.g., gelatin, BSA, Thesit, PEG-8000, glycerol, glucose, mannitol, galacitol, glucitol, and sorbitol) a stabilizer that, although not disclosed as such, might function as a non-ionic surfactant (e.g., Thesit).

Thus, although Park et al. disclose the combination of a polymerase, a sedimenting agent or a water-soluble dye, in the presence/absence of stabilizer, they provide no guidance for one of skill in the art to (i) select a *dye* from the choice of *a dye or a sedimenting*

agent (1 out of 2 choices), and (ii) select a stabilizer that, although not disclosed as such, might function as a *non-ionic surfactant* (e.g., Thesit) from the possibility of no stabilizer or one of the ten listed stabilizers (1 out of 11 choices) to arrive at *the combination of a polymerase, a dye, and a nonionic surfactant* (1 out of 22 choices).

SCHULTZ ET AL. FAIL TO DISCLOSE OR SUGGEST COMPOSITIONS THAT INCLUDE A DYE

Shultz et al. disclose "methods and compositions for protein stabilization, particularly the stabilization of polymerases in aqueous solutions with cationic surfactants. The activity of polymerases in solution, either in storage buffers or reaction buffers, may be stabilized by the addition of non-ionic surfactants" (column 6, lines 38-43). However, Shultz et al. fail to teach or suggest, among other things, any methods or compositions that include a dye. Thus, Schultz et al. also fail to teach or suggest stabilization of compositions that include a dye with non-ionic surfactants.

HAYES ET AL. FAIL TO DISCLOSE OR SUGGEST COMPOSITIONS THAT INCLUDE A SURFACTANT

Hayes et al. disclose "methods and apparatus for changing the temperature of material in a vessel by exposing the vessel to electromagnetic radiation" (column 1, lines 5-8). Hayes et al. further disclose the use of "heat absorptive dyes . . . for enhancing the heating effect of the electromagnetic radiation" (column 3, lines 10-12). However, Hayes et al. fail to teach or suggest, among other things, any methods or apparatuses that include a surfactant.

ONE OF SKILL IN THE ART WOULD HAVE NO MOTIVATION TO COMBINE PARK ET AL. IN VIEW OF SCHULTZ ET AL. AND HAYES ET AL. TO ARRIVE AT THE PRESENTLY CLAIMED INVENTION

Although documents can be combined in order to determine obviousness, "[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988). One cannot simply "engage in a hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps." *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991). Further, both the suggestion for combining the teachings of the prior art to make the invention and the reasonable likelihood of its success must be founded in the prior art and not in the teachings of Applicants' disclosure. *In re Dow Chem. Co.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). Applicants respectfully submit that the cited art neither suggests the combination of its teachings nor suggests the reasonable likelihood that such a combination would result in the presently claimed invention.

First, the Examiner alleged that "[i]t would have been obvious to include in the PCR reagent mixture of Park et al a nonionic surfactant to obtain its function to improve reactivity as taught by Park et al and to obtain its function to stabilize the polymerase as taught by Schultz et al." (page 5, lines 1-4, of the Office Action mailed November 19, 2003). Applicants respectfully traverse the Examiner's allegation. Applicants respectfully submit that, absent hindsight reconstruction, one of skill in the art would have no motivation to combine Park et al. with Schultz et al., to arrive at the presently claimed invention. For example, the present invention recites a composition in which a "dye inactivates the enzyme in the absence of the surfactant" (e.g., claims 1-19), or a method of stabilizing an enzyme in the presence of a dye "under conditions that normally inactivate the enzyme," wherein the method includes "combining an effective amount of a . . . surfactant . . . with the enzyme and the dye" (e.g., claims 20-24).

Applicants respectfully submit that one of skill in the art would have no motivation to combine Schultz et al., which fails to disclose or suggest stabilization of compositions that include a dye with non-ionic surfactants, with Park et al., which discloses dye-containing compositions. Further, Applicants respectfully submit that one of skill in the art would not have a reasonable expectation of success in combining Park et al. with Schultz et al. to stabilize an enzyme in the presence of a dye.

Second, the Examiner alleged that "[i]t would have been further obvious to include in the reagent mixture a heat absorptive dye to obtain its function of enhancing the heating effect of electromagnetic radiation as taught by Hayes et al. (page 5, lines 4-7, of the Office Action mailed November 19, 2003). Applicants respectfully traverse the Examiner's allegation. Applicants respectfully submit that, absent hindsight reconstruction, one of skill in the art would have no motivation to combine Park et al. in view of Schultz et al. with Hayes et al., to arrive at the presently claimed invention. Further, Applicants respectfully submit that Hayes et al., which fails to disclose or suggest any methods or apparatuses that include a surfactant, fail to correct the deficiencies of Park et al. in view of Schultz et al.

Finally, the Examiner alleged that "the dye of Park et al and/or the heat absorptive dye of Hayes et al would have *inherently* reduced polymerase activity in the absence of the surfactant" (page 5, lines 7-10, of Office Action mailed November 19, 2003, emphasis added). Applicants respectfully traverse the Examiner's allegation. Applicants respectfully reiterate that that Park et al., do not disclose, and in fact teach away from, a composition in which a "dye inactivates the enzyme in the absence of the surfactant" (e.g., claims 1-19), or a method of stabilizing an enzyme in the presence of a dye "under conditions that normally inactivate the enzyme," wherein the method includes "combining an effective amount of a . . . surfactant . . . with the enzyme and the dye" (e.g., claims 20-24). *See, for example*, the arguments in the paragraph spanning pages 6-7 of the Amendment and Response submitted by Applicants on 15 January 2003, which is incorporated herein by reference. The Examiner responded by asserting

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that "Applicants may be using a different method for determining a decrease in enzyme activity due to the dye than used by Park et al for determining a decrease in PCR level" (page 7, lines 3-5 of the Office Action mailed November 19, 2003). Applicants respectfully submit that the Examiner's response is not relevant to the present fact situation. No matter what method of measurement was used, Park et al., in referring to PCR compositions including dyes, stated that "there was no decrease in the level of PCR" (column 6, lines 16-17). Applicants respectfully submit that this is evidence that Park et al. do not disclose a composition in which a "dye inactivates the enzyme in the absence of the surfactant" (e.g., present claims 1-19), or a method of stabilizing an enzyme in the presence of a dye "under conditions that normally inactivate the enzyme" (e.g., claims 20-24).

Applicants respectfully submit that Park et al. in view of Shultz et al. and Hayes et al. fail to teach or suggest the presently claimed invention. Furthermore, Park et al., Shultz et al., and Hayes et al. provide no suggestion or motivation for one of skill in the art to modify or to combine their teachings to arrive at the present invention with a reasonable expectation of success.

The Examiner rejected claims 2-4, 17-19, 21, and 24 under 35 U.S.C. §103(a) as being unpatentable over Park et al. (U.S. Patent No. 5,861,251) in view of Shultz et al. (U.S. Patent No. 6,242,235 B1) and Hayes et al. (U.S. Patent No. 5,721,123) as applied to claims 1, 5-16, 20, and 23, and further in view of Nadeau et al. (U.S. Patent No. 5,919,630).

The deficiencies of Park et al. in view of Shultz et al. and Hayes et al., as applied to claims 1-24, have been discussed herein above.

Nadeau et al. disclose "methods for detecting nucleic acid target sequences" (column 1, lines 9-10). However, Nadeau et al. fail to disclose or suggest, among other things, any methods that include a surfactant. Thus, Nadeau et al. provide nothing to correct the deficiencies of Park et al. in view of Shultz et al. and Hayes et al. Furthermore, Applicants

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respectfully submit that one cannot simply engage in a hindsight reconstruction of the claimed invention, using Applicants' structure as a template and selecting elements from documents to fill the gaps.

Based on the remarks presented herein above, Applicants respectfully submit that claims 2-4, 17-19, 21, and 24 are patentable over Park et al. in view of Shultz et al. and Hayes et al., and further in view of Nadeau et al.

Applicants respectfully request that the rejections under 35 U.S.C. §103(a) be reconsidered and withdrawn.

Request for Rejoinder

Claims 25-50 have been withdrawn by the Examiner from further consideration as being drawn to non-elected inventions. Pursuant to M.P.E.P. §821.04, rejoinder of the non-elected claims is respectfully requested upon notice of allowable subject matter. Notably, independent claims 25, 31, 41, 45, 49, and 50, that have been withdrawn from further consideration, are method claims that recite the language of the composition of, for example, independent claim 1. Similarly independent claim 46 is a device claim that recites the language of the composition of, for example, independent claim 1. *See, for example, 1184 O.G. 86* citing *In re Ochiai*, 37 USPQ2d 1127 (Fed. Cir. 1995) and *In re Brouwer*, 37 USPQ2d 1663 (Fed. Cir. 1996).

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Summary

It is respectfully submitted that all the pending claims are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
Parthasarathy et al.

By

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CERTIFICATE UNDER 37 CFR §1.10::

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I hereby certify that the Transmittal Letter and the paper(s) and/or fee(s), as described hereinabove, are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR §1.10 on the date indicated above and is addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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